REMARKS

In the Office Action dated May 22, 2009, claims 1, 4-7 and 9 were examined with the result that all claims were rejected. Claims 3 and 8 were previously withdrawn from further consideration. The rejection of the claims was made non-final by the examiner. In response, Applicant has cancelled claim 9, amended claim 1, and submits the following remarks. In view of the above amendments and the following remarks, reconsideration of this application is requested.

Claim 1 has been amended to be limited to administering solely the compound 2-methylene-19-nor-20(S)-1α,25-dihydroxy vitamin D_3 (hereinafter referred to as "2MD") for treating ulcerative colitis. Support is found at page 7, lines 3-6 of the specification as filed as well as original claim 9. The amendment to claim 1 necessitated the cancelling of claim 9.

In the Office Action, claims 1, 4-7 and 9 were rejected under 35 U.S.C. §103(a) as being unpatentable over DeLuca et al US 5,843,928 in view of DeLuca et al WO 01/92221 and Hayes et al U.S. 6,358,939. The Examiner states that DeLuca et al '928 teaches the use of 2MD to treat various diseases, but fails to teach the use of 2MD to treat ulcerative colitis. However, the Examiner further states that DeLuca et al '221 teaches "very similar" vitamin D compounds useful in treating inflammatory bowel diseases, and although the DeLuca et al '221 reference fails to teach the specific treatment of ulcerative colitis as claimed, the Examiner utilizes Hayes et al to show that inflammatory bowel diseases are inclusive of ulcerative colitis. Thus, the Examiner concludes that it would be obvious to utilize the previously claimed compounds in the treatment of ulcerative colitis. Applicant, however, respectfully disagrees for the following reasons.

In the Office Action, the Examiner states that "absent evidence to the contrary," a person skilled in the art would have a reasonable expectation of successfully treating ulcerative colitis with the compound 2MD. However, it should be noted by the Examiner that a combination of DeLuca et al '928 together with DeLuca et al '221 and Hayes et al does not result in Applicant's claimed invention, i.e. the treatment of ulcerative colitis with 2MD. More specifically, DeLuca et al '928 teaches various uses for 2MD, but not the treatment of ulcerative colitis. DeLuca et al '221 teaches various vitamin D compounds to treat inflammatory bowel diseases, but does not teach the use of the compound 2MD to treat such inflammatory bowel diseases. Hayes et al teaches that ulcerative colitis is an inflammatory bowel disease, but does not teach the use of 2MD to treat ulcerative colitis. Thus, Applicant's claim 1 is novel over a combination of the references cited by the Examiner.

Also, Applicant has shown via the previous DeLuca Declaration filed with the response of September 23, 2008 that not all vitamin D compounds that have cell differentiation activity will also treat an intestinal bowel disease. The DeLuca Declaration tested four different vitamin D compounds and specifically concludes that, although all four compounds tested are vitamin D compounds and all four compounds have significant cell differentiation activity, only the compounds 1α,25-dihydroxy vitamin D_3 and 1AGR resulted in decreased inflammatory bowel disease, and the other two compounds tested, namely, DP035 and DP066 did not reduce inflammatory bowel disease. These latter two compounds, although vitamin D compounds and although having significant cell differentiation activity, will not result in being useful to treat inflammatory bowel disease such as ulcerative colitis. Finally, the Examiner should note that the data set forth in the present application show that the compound 2MD is effective to treat ulcerative colitis.

Applicants believe the Examiner's position that one skilled in the art would have a reasonable expectation of successfully treating ulcerative colitis with any vitamin D compound, including the compound 2MD, has been refuted in view of the above arguments and the previously supplied DeLuca Declaration. There is no guarantee that just because a compound is a vitamin D compound and that compound might have cell differentiation activity, that the compound will also treat ulcerative colitis. Thus, a combination of DeLuca et al '928 with DeLuca et al '221 and Hayes et al does not teach or suggest, and especially does not provide a reasonable expectation of success, of treating ulcerative colitis with all vitamin D compounds, much less the compound 2MD in view of the above arguments and previously supplied DeLuca Declaration.

In addition, the presently claimed compound 2MD has biological activities which give it an advantage over other vitamin D compounds for treating ulcerative colitis. More specifically, the compound 2MD has significantly less intestinal calcium transport activity than many other vitamin D compounds, and especially the 2-ethylidene compounds of the DeLuca et al '221 as well as the compound 1α,25-dihydroxy vitamin D_3 taught in the Hayes et al reference. The significance of this is that the compound 2MD can be administered to treat ulcerative colitis with significantly less risk of developing hypercalcemia from intestinal calcium transport activity. Therefore, the compound 2MD is less likely to result in hypercalcemia from intestinal calcium absorption upon administration at the same dosage as the 2-ethylidene compounds of the '221 reference or 1α,25-dihydroxy vitamin D_3 of the Hayes et al reference. This results in a compound that will treat ulcerative colitis, but yet at the same time have a safer window of toxicity to a patient.

In addition, the Examiner rejected claims 1, 6, 7 and 9 on the grounds of obviousness type double patenting as being unpatentable over claims 1, 5 and 8-11 of U.S. Patent 6,989,377. Although the conflicting claims were not identical, the Examiner alleges that they are not patentably distinct. Applicant respectfully disagrees with the Examiner.

With respect to U.S. Patent 6,989,377, the Examiner will note that this patent covers a method of treating ulcerative colitis and Crohn's disease with a vitamin D compound selected from 1α,25-dihydroxyvitamin D_3 or 1α-hydroxyvitamin D_3 in combination with an effective amount of interleukin-10. Broadly, the '377 patent refers to other vitamin D compounds as for example those represented by the formula found at column 4, lines 5-52. However, the Examiner will note that in the formula shown, the substituents Y^1 and Y^2 can either be hydrogen, or one can be O-aryl or O-alkyl while the other is hydrogen. Thus, the formula does not cover the presently-claimed 2MD compound, and as a result the present claims are novel over the '377 patent. In addition, Applicant refers the Examiner to the description found at column 19, line 65 through column 20, line 15. At this location, the '377 patent states:

> "...it is believed that the co-administration of IL-10 serves to counteract the calcemic effect of biologically active vitamin D compounds. As such, co-administering IL-10 to a subject helps prevent hypercalcemia from developing in the subject, and allows higher doses of biologically active vitamin D compounds to be

> tolerated by the subject. Importantly, this reduces the risk of using biologically active vitamin D compounds to treat vitamin D responsive diseases (e.g. risk a patient's dyeing [sic] from hypercalcemia), and also allow subjects to tolerate the higher doses that may be required to effectively treat certain vitamin D responsive diseases."

Thus, the '377 patent covers the idea of giving higher doses of active vitamin D compounds in combination with interleukin-10 in order to treat diseases because co-administering IL-10 helps prevent hypercalcemia from developing in the patient. In other words, without interleukin-10 there would be danger of administering toxic levels of vitamin D compounds to patients with the resultant hypercalcemia causing severe side effects, and possible death. In contrast, the present compound 2MD does not result in vitamin D intoxication at the recommended doses. This is because the present 2MD compound has significantly less intestinal calcium transport activity than the prior art vitamin D compounds, such as those set forth in the '377 patent. Thus, in view of what is taught in the '377 patent, one would expect to need to combine the present claimed compound with an immunomodulatory compound such as interleukin-10 in order to treat ulcerative colitis, but instead Applicant has discovered that the presently-claimed compound will treat the disease without resulting in vitamin D intoxication, at the lower recommended dosages. The Examiner should note claim 1 has been amended to use the phrase "consisting of" 2MD in order to answer the Examiner's issue that previous claim 1 did not exclude the use of interleukin-10. Thus, Applicant believes the presently-claimed invention is not obvious in view of the '377 patent.

Finally, the Examiner cites U.S. Patent 7,259,143 in a second obviousness type double patenting rejection. The '143 patent is directed toward a method of extending the dose range of vitamin D compounds by administering a vitamin D compound of the formula disclosed therein at a dosage sufficient to produce hypercalcemia, i.e. a toxic dose, in combination with also administering a bone calcium absorption inhibitor such as a bisphosphonate. This reference is similar to U.S. Patent 6,989,377 in that high doses of vitamin D compounds are being administered to treat a disease and a second agent is being co-administered to counteract the calcemic effect of the vitamin D compound. In the '377 patent it was interleukin-10. In the '143 patent it is a bone calcium absorption inhibitor such as a bisphosphonate (see claim 11 of the '143 patent). See also column 1, line 51 through column 2, line 48. Thus, once again, the '143 patent teaches one skilled in the art that a combination of a vitamin D compound and a bone calcium resorption inhibitor is necessary in order to treat a disease such as IBD. However, Applicant has found that the presently-claimed compound 2MD will treat the disease and not result in hypercalcemia at the recommended lower dosages since the presently-claimed compound has relatively low intestinal calcium transport activity. Again, Applicant notes that claim 1 has been amended to use the phrase "consisting of" to exclude bone calcium resorption inhibitors.

Accordingly, applicant requests the Examiner withdraw the §103(a) rejection as well as all of the double patenting rejections.

An effort has been made to place this application into condition for allowance and such action has been earnestly requested.

Respectfully submitted,

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